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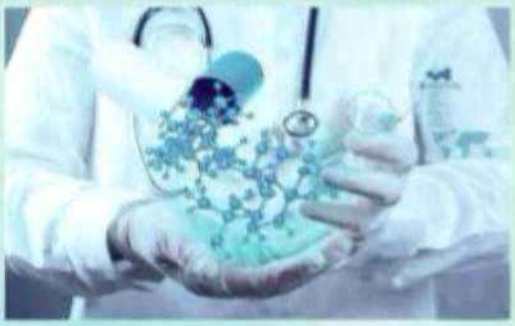

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НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
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HOW GENETIC VARIATIONS IN ESR1 IMPACT PROSTATE CANCER AND BENIGN PROSTATIC HYPERPLASIA

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✓ ***Resume***

Polymorphism PvuII (rs2234693) in the ESR1 gene (estrogen receptor alpha) may play a significant role in the pathogenesis of benign prostatic hyperplasia (BPH) and prostate cancer (PCa). This single nucleotide polymorphism (T/C) can modulate ESR1 expression and receptor activity, thereby influencing tissue responses to estrogens, cell proliferation, apoptosis, and inflammation within the prostate. In this study, we evaluated the distribution of the T (major) and C (minor) alleles and corresponding genotypes (T/T, T/C, C/C) among patients with lower urinary tract symptoms (LUTS) due to BPH and PCa and compared them to healthy controls. Our findings indicate that the minor C allele is more frequent among affected patients, suggesting an association with increased susceptibility to prostate pathology. These results highlight potential value of the ESR1 PvuII polymorphism as a biomarker for risk stratification and as a candidate for personalized preventive and therapeutic strategies in prostate disorders.

Keywords:

ESR1, estrogen receptor alpha, PvuII polymorphism, rs2234693, benign prostatic hyperplasia, prostate cancer, genetic susceptibility, biomarkers, LUTS, genetic variations.

КАК ГЕНЕТИЧЕСКИЕ ВАРИАЦИИ В ESR1 ВЛИЯЮТ НА РАК ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ И ДОБРОКАЧЕСТВЕННУЮ ГИПЕРПЛАЗИЮ ПРОСТАТЫ

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✓ ***Резюме***

Полиморфизм PvuII (rs2234693) в гене ESR1 (эстрогеновый рецептор α) может играть значимую роль в патогенезе доброкачественной гиперплазии простаты (ДГПЖ) и рака предстательной железы (РПЖ). Этот однонуклеотидный полиморфизм (T/C) способен модулировать экспрессию ESR1 и активность рецептора, влияя на тканевые реакции на эстрогены, клеточную пролиферацию, апоптоз и воспалительные процессы в ткани простаты. В данном исследовании мы оценили распределение основных (T) и минорных (C) аллелей, а также соответствующих генотипов (T/T, T/C, C/C) среди пациентов с симптомами нижних мочевых путей (СНМП), обусловленными ДГПЖ и РПЖ, и сравнили их со здоровыми контрольными группами. Наши результаты показывают, что минорный аллель C встречается чаще у пациентов с патологией, что предполагает его возможную

ассоциацию с повышенной предрасположенностью к заболеваниям простаты. Эти данные подчеркивают потенциальную ценность полиморфизма PvuII гена ESR1 как биомаркера для стратификации риска и как перспективного кандидата для разработки персонализированных профилактических и терапевтических подходов при патологии предстательной железы.

Ключевые слова: ESR1, эстрогеновый рецептор α, полиморфизм PvuII, rs2234693, доброкачественная гиперплазия простаты, рак предстательной железы, генетическая предрасположенность, биомаркеры, СНМП, генетические вариации.

ESR1 GENIDAGI GENETIK VARIATSIYALAR PROSTATA BEZI SARATONI VA PROSTATA BEZI XAVFSIZ GIPERPLAZIYASIGA QANDAY TA'SIR QILADI

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✓ ***Rezyume***

ESR1 genidagi PvuII (rs2234693) polimorfizmi (estrogen retseptori α) prostata bezi havfsiz giperplaziyasi va prostata bezi saratoni (PBS) patogenezida muhim rol o'ynashi mumkin. Ushbu bir nukleotidli polimorfizm (T/C) ESR1 genining ekspressiyasini va retseptor faolligini modulyatsiya qilishi orqali estrogenlarga bo'lgan to'qima javobini, hujayra proliferatsiyasini, apoptozni hamda prostata to'qimasidagi yallig'lanish jarayonlarini o'zgartirishi mumkin. Ushbu tadqiqotda biz asosiy (T) va minor (C) allellarning, shuningdek, mos genotiplarning (T/T, T/C, C/C) PBHG va PBS tufayli pastki siydik yo'llari simptomlariga (PSYS) ega bo'lgan bemorlar orasida tarqalishini baholadik va ularni sog'lom nazorat guruhi bilan solishtirdik. Natijalarimiz shuni ko'rsatdiki, minor C alleli ushbu patologiyalarga ega bemorlar orasida ko'proq uchraydi, bu esa uning prostata kasalliklariga moyillikni oshiruvchi omil bo'lishi mumkinligini bildiradi.

Kalit so'zlar: ESR1, alfa estrogen retseptori, PvuII polimorfizmi, rs2234693, prostata bezi saratoni, genetik moyillik, biomarkyerlar, pastki siydik yo'llari simptomlari (PSYS), genetik variatsiyalar..

Introduction

Estrogen signaling via estrogen receptor alpha (ESR1) influences prostate development and homeostasis and contributes to pathophysiological processes linked to BPH and prostate cancer. The ESR1 PvuII polymorphism (rs2234693, T→C) has been studied in various hormone-sensitive tissues and implicated in altering receptor expression and function. Given estrogens' role in stromal–epithelial interactions, inflammation, and cellular proliferation in the prostate, variants in ESR1 may modulate individual susceptibility to benign and malignant prostate disease.

This study aims to assess the frequency of the ESR1 PvuII alleles and genotypes in patients with BPH and PCa compared to healthy controls, using the same clinical cohort and methodology framework as in our template study.

Materials and methods

Study subjects. The present study included 74 men who visited the clinic for LUTS between January 2022 and December 2023. Clinical assessment used the International Prostate Symptom Score (IPSS) and quality of life (QoL) questionnaires. Prostate volumes were measured by transrectal ultrasonography and serum prostate-specific antigen (PSA) concentrations determined. Peak urine flow velocity (Qmax) and average flow (Qavg) were measured by uroflowmetry.

Genotyping and laboratory methods. Blood samples were collected into EDTA tubes. Genomic DNA was extracted by standard protocols. Genotyping of ESR1 PvuII (rs2234693, T/C) was performed by PCR-based methods followed by restriction fragment length polymorphism analysis or real-time PCR allelic discrimination on thermal cyclers (Applied Biosystems 2720 and Rotor-Gene Q). All procedures followed GRIPS recommendations to ensure transparency and reproducibility of genetic association reporting. Standard laboratory consumables (Vacutainer EDTA tubes, etc.) were used.

Study design and groups. A case-control model was applied. Subjects with neurogenic bladder, urethral stricture, acute/chronic prostatitis, urinary tract infection, uncontrolled diabetes mellitus, prior pelvic surgery, or uncontrolled hypertension were excluded. Subjects were classified into: control group (prostate volume <30 mL, minimal LUTS), BPH group (prostate volume ≥30 mL; IPSS >8; Qmax <15 mL/sec), and PCa group where applicable (histologically confirmed). All participants provided written informed consent.

Statistical analysis. Allele and genotype frequencies were calculated; chi-square (χ^2) tests determined significance of differences between groups. Odds ratios (OR) with 95% confidence intervals (CI) were computed. $p < 0.05$ was considered statistically significant.

Result and discussions

Allele and genotype distribution (overall sample). In the study cohort, the T (major) allele accounted for 85.8% and the C (minor) allele 14.2%. Genotype distribution in patients showed T/T in 74.5%, T/C in 22.6%, and C/C in 2.8%. In the control group (n = 105), the T allele frequency was 93.3%, C allele 6.7%, with genotypes T/T 86.7%, T/C 13.3%, and no C/C observed.

Comparison between patient and control groups demonstrated that the C minor allele occurred significantly more frequently among patients ($\chi^2 = 6.3$; $p = 0.03$; OR = 2.3; 95% CI: 1.2–4.43), suggesting its possible involvement in predisposition to prostate disease. The T allele was associated with lower risk ($\chi^2 = 6.3$; $p = 0.03$; OR = 0.4; 95% CI: 0.23–0.83). The T/T genotype appeared protective ($\chi^2 = 5.0$; $p = 0.05$; OR = 0.5; 95% CI: 0.22–0.91), whereas carriage of T/C showed a non-significant trend toward increased risk (OR = 1.9; $\chi^2 = 3.1$; $p = 0.10$).

BPH vs controls. Among patients with BPH, the T allele frequency was 87.8%, C allele 12.2%; genotype T/T 77.0%, T/C 21.6%, C/C 1.4%. Compared to controls, the differences did not reach statistical significance (T: $\chi^2 = 3.2$; $p = 0.10$; OR = 0.5; 95% CI: 0.25–1.06), but the C allele and heterozygous genotype were observed more often in BPH patients (C: 12.2% vs 6.7%; T/C: 21.6% vs 13.3%), suggesting a possible initiating effect that merits study in larger cohorts.

PCa vs controls. In patients with prostate cancer, the C allele frequency was higher (18.8%) compared with controls (6.7%) and the difference was statistically significant ($\chi^2 = 8.3$; $p = 0.01$; OR = 3.2; 95% CI: 1.46–7.16). The T/T genotype was less frequent in PCa patients (68.8% vs 86.7% in controls) and conferred reduced risk ($\chi^2 = 5.4$; $p = 0.03$; OR = 0.3; 95% CI: 0.14–0.84). The T/C heterozygote was more common among PCa patients (25.0% vs 13.3%; OR = 2.2), although this did not reach statistical significance in this sample ($\chi^2 = 2.5$; $p = 0.20$; 95% CI: 0.83–5.68).

Summary of key findings. The ESR1 PvuII C allele and T/C genotype show an association with increased frequency in patients with prostate disease, most marked in the prostate cancer subgroup, while the T/T genotype and T allele display a protective association in this cohort.

(See Tables 1–5 for detailed allele/genotype counts, χ^2, p-values, OR and 95% CI — formatted analogous to the template document).

Discussion

This analysis indicates that the ESR1 PvuII polymorphism (rs2234693) may modulate prostate disease risk. Estrogen signaling through ESR1 influences stromal remodeling, inflammation, and epithelial proliferation — processes central to BPH pathogenesis and tumorigenesis. The C allele has been previously associated in some studies with altered ESR1 expression and hormone responsiveness; our findings showing higher C allele frequency among PCa patients support the hypothesis that ESR1 variation contributes to malignant transformation or progression in a subset of patients. The protective association of the T/T genotype is concordant with the lower frequency of the C allele in healthy controls observed here.

Limitations include moderate sample size and single-center design; larger multicenter studies and functional assays are required to confirm causality and to elucidate mechanistic links between ESR1 variants and prostate pathobiology.

Conclusion

The ESR1 PvuII (rs2234693) polymorphism demonstrates a pattern of association with BPH and PCa in our cohort: the minor C allele and heterozygous genotype are more frequent among patients, with strongest association seen in prostate cancer cases, while the T allele and T/T genotype show a protective effect. ESR1 polymorphism profiling may offer supplementary risk information for personalized management of prostate diseases, but further validation is necessary.

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